Moreover, the major portion of the new formula is obtained by simply combining the Formulas (1) and (2), which combination is claimed in original multidependent claim 8 insofar as it depends on original claim 7.

The hydrogen atom bound to the R_8 substituent in this new formula is supported by compounds 3, 4, 6, 7 and 9 in Example 1 of applicants' specification.

To react a compound of the new formula with hyaluronic acid and a dehydrative condensation agent (or a dehydrative condensation agent and a reaction accelerating additive) in order to obtain a compound according to the present invention is supported by the description at pages 31-36 of applicants' specification, as well as the Examples.

Applicants respectfully await the results of an examination on the merits including a consideration of the new claims as amended above.

Respectfully submitted,

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Version with Markings to Show Changes Made

1. A conjugate of (1) at least one therapeutic agent for joint diseases and (2) ~~hyaluroic~~ hyaluronic acid, a ~~hyaluroic~~ hyaluronic acid derivative or a salt thereof.

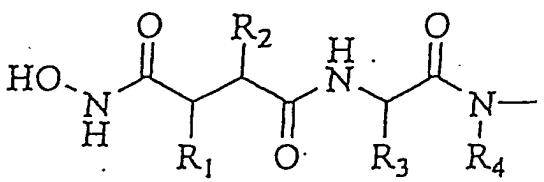
2. The conjugate of claim 1, wherein the bond between at least one therapeutic agent for joint diseases and ~~hyaluroic~~ hyaluronic acid, a ~~hyaluroic~~ hyaluronic acid derivative or a salt thereof is a covalent bond.

4. The conjugate of claim 3~~1~~, wherein the matrix metalloprotease inhibitor binds to ~~hyaluroic~~ hyaluronic acid, a ~~hyaluroic~~ hyaluronic acid derivative or the salt thereof via a spacer.

5. The conjugate of claim ~~1~~3, wherein the weight ratio of the matrix metalloprotease inhibitor to the entire conjugate is 0.01 to 50%.

6. The conjugate of claim ~~1~~3, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue.

7. The conjugate of claim ~~1~~3, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue represented by the general formula (1):



(1)

wherein

R_1 is a hydrogen atom, a hydroxyl group or a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

R_2 is a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

R_3 is a straight chain or branched alkyl group having 1 to 8 carbon atoms which may be substituted with a cycloalkyl group, an aryl group or a heterocyclic group; and

R_4 is a hydrogen atom or an alkyl group having 1 to 4 carbon atoms.

8. The conjugate of claim ~~1~~4, wherein the spacer is represented by the general formula (2):

$$-R_5-R_6-R_7-R_8- \qquad (2)$$

wherein

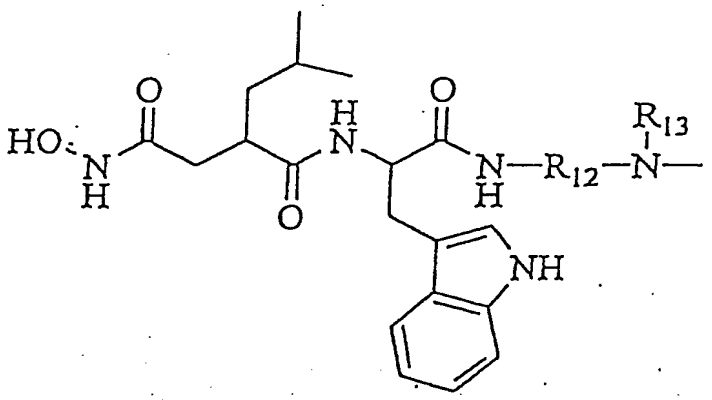
R_5 is a straight-chain or branched-chain alkylene group having 1 to 8 carbon atoms;

R_6 is an oxygen atom or a methylene or imino group which may be substituted with a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms;

R_7 is a straight-chain or branched-chain alkylene group having 1 to 10 carbon atoms into which one to three oxygen atoms may be inserted; and

R_8 is an oxygen atom, a sulfur atom or NR_9 wherein R_9 is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

9. The conjugate of claim ~~1~~4, wherein the conjugate of the matrix metalloprotease inhibitor and the spacer is represented by the general formula (3):



(3)

wherein

R_{12} is a straight-chain or branched-chain alkylene group having 2 to 23 carbon atoms into which one imino group and/or one to four oxygen atoms may be inserted; and

R_{13} is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

10. The conjugate of claim ~~1~~3, wherein the matrix metalloprotease inhibitor in the form of a conjugate with ~~hyaluroic~~ hyaluronic acid, a ~~hyaluroic~~ hyaluronic acid derivative or a salt thereof inhibits a matrix metalloprotease *in situ*.

11. A method for preparing the conjugate of claim 1 comprising binding a site of the therapeutic agent for joint diseases that does not affect the activity of the agent to a carboxyl group, a hydroxyl group or a functional group at the reducing end of ~~hyaluroic~~ hyaluronic acid, a ~~hyaluroic~~ hyaluronic acid derivative or a salt thereof by direct chemical reaction or via a spacer.